**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re the Application of: **Hiroyuki OHNO** Art Unit: **1634**

Application Number: **10/593,898** Examiner: **Ethan C. Whisenant**

Filed: **September 22, 2006** Confirmation Number: **4742**

For: **SOLVENT FOR DISSOLVING NUCLEIC ACID, NUCLEIC ACID-CONTAINING SOLUTION AND METHOD OF PRESERVING NUCLEIC ACID**

Attorney Docket Number: **063057**
Customer Number: **38834**

## SUBMISSION OF APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

February 5, 2009

Sir:

Applicants submit herewith an Appeal Brief in the above-identified U.S. patent application.

Attached please find a check in the amount of $540.00 to cover the cost for the Appeal Brief. If any additional fees are due in connection with this submission, please charge Deposit Account No. 50-2866.

Respectfully submitted,

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# APPEAL BRIEF FOR THE APPELLANT

Ex parte Hiroyuki OHNO et al. (Applicant)

SOLVENT FOR DISSOLVING NUCLEIC ACID, NUCLEIC ACID-CONTAINING SOLUTION AND METHOD OF PRESERVING NUCLEIC ACID

Application Number: 10/593,898

Filed: September 22, 2006

Appeal No.:

Art Unit: 1634

Examiner: Ethan C. Whisenant

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# BRIEF ON APPEAL

## (I) REAL PARTIES IN INTEREST

The real parties in interest are **Hiroyuki OHNO** and **Nishinbo Industries, Inc.**, by an assignment recorded in the U. S. Patent and Trademark Office on **September 22, 2006**, at Reel **018355**, Frame **0335**.

## (II) RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellants, Appellants' legal representative, or assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

## (III) STATUS OF CLAIMS

Claims 1 and 3-14 are pending in the application. Claim 2 is cancelled. Claims 1 and 3-14 are rejected, and are appealed. The appealed claims are listed in the appendix.

## (IV) STATUS OF AMENDMENTS

No amendments have been filed subsequent to the close of prosecution.

## (V) SUMMARY OF THE CLAIMED SUBJECT MATTER

Claim 1 is directed at a solvent for dissolving nucleic acids, comprising an ionic liquid which can dissolve nucleic acids (*e.g.*, page 6, line 36 to page 7, line 9). The ionic liquid comprises at least one cation selected from the group consisting of imidazolium cations and pyridinium cations (*e.g.*, page 7, line 11 to page 8, line 24) and an anion which is selected from the group consisting of $BF_4^-$, $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, a halide ion and a carboxylic acid ion having a total of 1 to 3 carbons (*e.g.*, page 8, lines 26-32).

Claim 6 is directed at a nucleic acid-containing solution, comprising nucleic acids dissolved in an ionic liquid (*e.g.*, page 9, lines 6-9; page 18, lines 11-19; page 18 lines 29-31).

Claim 7 is directed at a method for preserving nucleic acids, comprising the step of preserving nucleic acids in a dissolved state within an ionic liquid for a long term (*e.g.*, page 11, line 29 to page 12, line 8).

Claim 11 is directed at a method of dissolving nucleic acids, comprising the step of dissolving nucleic acids with an ionic liquid which can dissolve nucleic acids (*e.g.*, page 9, lines 16-24). The ionic liquid comprises at least one cation selected from the group consisting of imidazolium cations and pyridinium cations (*e.g.*, page 7, line 11 to page 8, line 24) and an anion which is selected from the group consisting of $BF_4^-$, $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, a halide ion and a carboxylic acid ion having a total of 1 to 3 carbons (*e.g.*, page 8, lines 26-32).

## (VI) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 7-9 are indefinite under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Whether claims 1, 3-6 and 10-14 are anticipated under 35 U.S.C. §102(b) as being anticipated by Ohno et al.

Whether claims 7 and 8 are anticipated under 35 U.S.C. §102(b), or in the alternative, obvious under 35 U.S.C. 103(a) in view of Ohno et al.

## (VII) ARGUMENT

**35 U.S.C. §112, second paragraph, rejection of claims 7-9 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

It is the position of the Examiner that the phrase "for a long term" is a relative term and that the metes and bounds of what is intended cannot be determined. In response, Appellants respectfully submit that the fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). If a relative term is recited, such as "for a long term," a determination must be made as to whether one of ordinary skill in the art, in view of the specification, would nevertheless be reasonably apprised of the scope of the claim. See MPEP §2173.05(b).

Appellants respectfully note that the Examiner did not illustrate any such determination in the Office Action dated July 29, 2008. The specification discusses that conventional nucleic acid preservation techniques using water as a solvent are not viable for long-term preservation due to the evaporation of water. See page 3, line 1 to page 4, line 10. Accordingly, Appellants respectfully submit that one having ordinary skill in the art would be reasonably apprised of the scope of "for a long term" in the context of nucleic acid preservation and the evaporation of water solvents.

As to claims 8 and 9, Appellants respectfully submit that these claims should be objected to as being dependent upon a rejected base claim, rather than being rejected. Even if, *arguendo*, the claim "long term" of claim 7 is indefinite, claims 8 and 9 provide for unquestionably definite scope of time. In any event, Appellants respectfully submit that these claims are patentable at least due to their dependency on claim 7, which Appellants submit is patentable for at least the above reason. Therefore, for at least the foregoing reasons, Appellants respectfully submit that claims 7-9 are not being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**35 U.S.C. §102(b) rejection of claims 1, 3-6 and 10-14 as being anticipated by Ohno et al.**

It is the position of the Office Action that Ohno discloses the embodiments as claimed. Ohno is co-authored by one of the inventors, and is directed at ion conductive characteristics of DNA film containing ionic liquids. As a first step, Ohno discloses that ethylimidazolium

tetrafluoroborate ($EtImBF_4$) is evaporated to remove water and $HBF_4$. Page E168, column 2, first partial paragraph, lines 10-15. Then, the solution is washed with diethyl ether twice and dried *in vacuo* for four days. Page E168, column 2, first partial paragraph, lines 15-16. Next, $EtImBF_4$ is mixed with DNA and water. Page E168, column 2, first full paragraph, lines 1-2. This mixture is then cast on a Teflon plate and dried *in vacuo* for four days to obtain a flexible film. Page E168, column 2, first full paragraph, lines 3-4. As illustrated at the top of the first column on page E169, $EtImBF_4$ contains an imidazolium cation and a $BF_4^-$ anion.

Independent claim 1

Appellants first discuss the subject matter of claim 1. Ohno discloses a DNA film formed from a composition comprising $EtImBF_4$, DNA and water. The DNA is cast on a Teflon plate to form a film, and only exists in a solid state in the film. Ohno does not disclose that the DNA is dissolved in $EtImBF_4$. Rather, $EtImBF_4$ is only mixed with the DNA in a liquid state prior to casting the film.

On the other hand, claim 1 recites a solvent for dissolving nucleic acids containing an ionic liquid that can dissolve nucleic acids. The specification discusses what is meant by "dissolved" at page 7, lines 20-28. Specifically, "dissolved" means that the DNA will be in a clear and homogeneous solution after heating, but will remain precipitation-free at room temperature. Therefore, since Ohno does not disclose or suggest that $EtImBF_4$ dissolves nucleic acids, Appellants respectfully submit that Ohno does not disclose or suggest the subject matter of claim 1.

Independent claim 11

Next, Appellants discuss the subject matter of claim 11. As noted above, Ohno discloses a DNA film formed from a composition comprising $EtImBF_4$, DNA and water. The DNA is cast on a Teflon plate to form a film, and only exists in a solid state in the film. Ohno does not disclose that the DNA is dissolved in $EtImBF_4$. Rather, $EtImBF_4$ is only mixed with the DNA in a liquid state prior to casting the film.

On the other hand, claim 11 recites a method of dissolving nucleic acids containing a step of "dissolving." The specification discusses what is meant by "dissolved" at page 7, lines 20-28. Specifically, "dissolved" means that the DNA will be in a clear and homogeneous solution after heating, but will remain precipitation-free at room temperature. Therefore, since Ohno does not disclose or suggest that $EtImBF_4$ dissolves nucleic acids, Applicants respectfully submit that Ohno does not disclose or suggest the subject matter of claim 11.

Dependent claims 3 and 10

Next, Appellants discuss the subject matter of dependent claims 3 and 10, each of which recites a smaller Markush group than independent claim 1. First, Appellants respectfully submit that claims 3 and 10 are patentable at least due to their dependency on independent claim 1, which Appellants submit is patentable for at least the reasons discussed above.

Additionally, Appellants respectfully submit that Ohno does not disclose or suggest the subject matter of these claims. These claims do not recite that the solvent can include a $BF_4^-$

anion, but do recite a that it can include "halide ion." It is the position of the Examiner that that "$BF_4^-$ is a halide ion." See pages 4 and 5 of July 29, 2008 Office Action. However, Appellants respectfully submit this is incorrect—$BF_4^-$ is not a halide ion. In the Office Action dated July 29, 2008, the Examiner cited to a Wikipedia definition of "Halide." The Examiner modifies a quotation from this Wikipedia entry as follows (Examiner's additions in bold):

> A halide is a binary compound, of which one part is a halogen atom **(e.g. F)** and the other part is an element or radical that is less electronegative than the halogen **(e.g. B)**.

The citation provided by the Examiner also states that:

> A halide ion is a halogen atom bearing a negative charge. The halide anions are fluoride ($F^-$), chloride ($Cl^-$), bromide ($Br^-$), iodide ($I^-$) and astatide ($At^-$). Such ions are present in all ionic halide salts.

See page 5 of July 29, 2008 Office Action. The Examiner's interpretation specifically contradicts the Wikipedia citation, which states that: "The halide anions are fluoride ($F^-$), chloride ($Cl^-$), bromide ($Br^-$), iodide ($I^-$) and astatide ($At^-$)." Emphasis added. In other words, there are only five possible halide ions, and $BF_4^-$ is not one of them. Although $BF_4^-$ has a negative charge and includes a halogen, it is not is a "halide ion."

As further evidence of this fact, it is noted that the anion Markush group of claims 1 and 11 includes both $BF_4^-$ and a halide ion. If the Examiner's assertion was accurate, then these claims would include redundant subject matter. However, the claims were not objected to or rejected as containing redundant subject matter. Since Ohno only discloses a $BF_4^-$ anion, and this $BF_4^-$ anion is not among the anions recited in claims 3 and 10, Ohno cannot anticipate these claims.

Dependent claims 12 and 13

Next, Appellants discuss the subject matter of dependent claims 12 and 13, each of which recites a smaller Markush group than independent claim 11. First, Appellants respectfully submit that claims 12 and 13 are patentable at least due to their dependency on independent claim 11, which Appellants submit is patentable for at least the reasons discussed above.

Additionally, Appellants respectfully submit that Ohno does not disclose or suggest the subject matter of these claims. These claims do not recite that the solvent can include a $BF_4^-$ anion, but do recite that it can include a "halide ion." It is the position of the Examiner that that "$BF_4^-$ is a halide ion." See pages 4 and 5 of July 29, 2008 Office Action. However, Appellants respectfully submit this is incorrect—$BF_4^-$ is not a halide ion. In the Office Action dated July 29, 2008, the Examiner cited to a Wikipedia definition of "Halide." The Examiner modifies a quotation from this Wikipedia entry as follows (Examiner's additions in bold):

> A halide is a binary compound, of which one part is a halogen atom **(e.g. F)** and the other part is an element or radical that is less electronegative than the halogen **(e.g. B)**.

The citation provided by the Examiner also states that:

> A halide ion is a halogen atom bearing a negative charge. The halide anions are fluoride ($F^-$), chloride ($Cl^-$), bromide ($Br^-$), iodide ($I^-$) and astatide ($At^-$). Such ions are present in all ionic halide salts.

See page 5 of July 29, 2008 Office Action. The Examiner's interpretation specifically contradicts the Wikipedia citation, which states that: "The halide anions are fluoride ($F^-$), chloride ($Cl^-$), bromide ($Br^-$), iodide ($I^-$) and astatide ($At^-$)." Emphasis added. In other words,

there are <u>only</u> five possible halide ions, and $BF_4^-$ is <u>not</u> one of them. Although $BF_4^-$ has a negative charge and includes a halogen, it is not is a "halide ion."

As further evidence of this fact, it is noted that the anion Markush group of claims 1 and 11 includes both $BF_4^-$ and a halide ion. If the Examiner's assertion was accurate, then these claims would include redundant subject matter. However, the claims were not objected to or rejected as containing redundant subject matter. Since Ohno only discloses a $BF_4^-$ anion, and this $BF_4^-$ anion is not among the anions recited in claims 12 and 13, Ohno cannot anticipate these claims.

<u>Claim 6</u>

Next, Appellants discuss claim 6, which recites a nucleic acid solution comprising "nucleic acids dissolved in an ionic liquid." The specification discusses what is meant by "dissolved" at page 7, lines 20-28. Specifically, "dissolved" means that the DNA will be in a clear and homogeneous solution after heating, but will remain precipitation-free at room temperature.

However, Ohno does not state that DNA is "dissolved" in $EtImBF_4$. In Ohno, the nucleic acids are preserved in a dried (or drying) film. A dried (or drying) film is not a "dissolved state," since the DNA is not in a homogeneous solution. Thus, Ohno does not disclose a nucleic acid solution comprising "nucleic acids dissolved in an ionic liquid." Therefore, for at least the foregoing reasons, Appellants respectfully argue that claims 1, 3-6 and 10-14 are not anticipated by Ohno.

**35 U.S.C. §§102/103 rejection of claims 7 and 8 as being anticipated by or, in the alternative, as obvious over Ohno.**

It is the position of the Office Action that Ohno discloses the method as claimed, with the exception of explicitly teaching that "the nucleic acid dissolved in their ionic liquid is preserved." Page 7 of July 29, 2008 Office Action. The Examiner argues that this is inherent to Ohno. The Examiner also refers to Figure 2 on page E169. The Examiner states that "If the nucleic acids within the ionic liquids were not preserved during the drying step (i.e., they were degraded) a signal similar to that of ionic liquid alone would have been seen." As to the duration of preservation, the Examiner states that Ohno teaches "drying their DNA films for 4 days (i.e., at least 48 hours)."

As discussed above, Ohno is directed at ion conductive characteristics of DNA film containing ionic liquids. As a first step, Ohno discloses that ethylimidazolium tetrafluoroborate ($EtImBF_4$) is evaporated to remove water and $HBF_4$. Page E168, column 2, first partial paragraph, lines 10-15. Then, the solution is washed with diethyl ether twice and dried *in vacuo* for four days. Page E168, column 2, first partial paragraph, lines 15-16. Next, $EtImBF_4$ was mixed with DNA and water. Page E168, column 2, first full paragraph, lines 1-2. This mixture is then cast on a Teflon plate and dried *in vacuo* for four days to obtain a flexible film. Page E168, column 2, first full paragraph, lines 3-4. As illustrated at the top of the first column on page E169, $EtImBF_4$ contains an imidazolium cation and a $BF_4^-$ anion.

First, Appellants respectfully submit that claims 7 and 8 recite "preserving nucleic acids in a dissolved state." The specification discusses what is meant by "dissolved" at page 7, lines

20-28. Specifically, "dissolved" means that the DNA will be in a clear and homogeneous solution after heating, but will remain precipitation-free at room temperature. However, in Ohno, the nucleic acids are preserved in a dried (or drying) film. A dried (or drying) film is not a "dissolved state," since the DNA is not in a homogeneous solution. Thus, Ohno does not disclose "preserving nucleic acids in a dissolved state," as required by claims 7 and 8.

Additionally, as noted above, the Examiner refers to Figure 2, and states that if the DNA was degraded, the ionic conductivity of ionic liquid alone and the ionic liquid with DNA would have been the same. In other words, the Examiner states that since the open circles and closed circles in Figure 2 are not overlapping, the DNA must be preserved. Appellants note that Ohno does not discuss this point; the Examiner's statement appears to be his own hypothesis.

Appellants respectfully submit that this is not accurate. An ionic liquid containing degraded DNA would still contain a large number of individual nucleic acids or small sequences of nucleic acids. As such, the content, and thus the ionic conductivity, of a pure ionic liquid and an ionic liquid containing degraded DNA would be different.

Additionally, independent of whether or not DNA was preserved, the conductivity of an ionic liquid in a film would be different from pure ionic liquid. The number of ions derived from ionic liquid in a film (ionic content: 88.5 wt%) is less than that in pure ionic liquid. Accordingly, it is clear that the ionic conductivity of a film is lower than that of pure ionic liquid. Therefore, even if the film did not contain any nucleic acids, the values for the open and closed circles in Figure 2 would have different levels of ionic conductivity.

In other words, the difference between the open circles and closed circles in Figure 2 could be due to (i) attributed to the difference in ionic conductivity between ionic liquid in a film containing no nucleic acids and pure ionic liquid, or (ii) attributed to the difference in ionic conductivity between ionic liquid in a film containing partially degraded DNA and a pure ionic liquid. Thus, Figure 2 does not necessarily indicate that the nucleic acids have been preserved. For at least the foregoing reasons, Appellants respectfully argue that claims 7 and 8 are not anticipated by or, in the alternative, obvious over Ohno.

## CONCLUSION

For at least the foregoing reasons, the Examiner has failed to raise a *prima facie* rejection of the claims. The Honorable Board is respectfully requested to reverse the rejection.

If this paper is not timely filed, appellants hereby petition for an appropriate extension of time. The fee for any such extension may be charged to Deposit Account No. 50-2866, along with any other additional fees that may be required with respect to this paper.

Respectfully submitted,

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## (VII) CLAIMS APPENDIX

1. A solvent for dissolving nucleic acids, comprising:

an ionic liquid which can dissolve nucleic acids, said ionic liquid comprising:

at least one cation selected from the group consisting of imidazolium cations and pyridinium cations, and

an anion which is selected from the group consisting of $BF_4^-$, $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, a halide ion and a carboxylic acid ion having a total of 1 to 3 carbons.

3. The solvent for dissolving nucleic acids of claim 1 or 10, wherein said anion is selected from the group consisting of said halide ion and said carboxylic acid ion having a total of 1 to 3 carbons.

4. The solvent for dissolving nucleic acids of claim 1 or 10, wherein the ionic liquid is a neutralized ionic liquid.

5. The solvent for dissolving nucleic acids of claim 1 or 10, wherein said solvent is adapted to preserve nucleic acids or to react nucleic acids.

6. A nucleic acid-containing solution, comprising nucleic acids dissolved in an ionic liquid.

7. A method for preserving nucleic acids, comprising the step of preserving nucleic acids in a dissolved state within an ionic liquid for a long term.

8. The method for preserving nucleic acids of claim 7, wherein said long term is at least 48 hours.

9. The method for preserving nucleic acids of claim 7, wherein said long term is at least 120 hours.

10. The solvent for dissolving nucleic acids of claim 1, wherein said anion is selected from the group consisting of $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, said halide ion and said carboxylic acid ion having a total of 1 to 3 carbons.

11. A method of dissolving nucleic acids, comprising the step of:

dissolving nucleic acids with an ionic liquid which can dissolve nucleic acids,

wherein said ion liquid comprises:

at least one cation selected from the group consisting of imidazolium cations and pyridinium cations, and

an anion which is selected from the group consisting of $BF_4^-$, $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, a halide ion and a carboxylic acid ion having a total of 1 to 3 carbons.

12. The method of dissolving nucleic acids of claim 11, wherein said anion is selected from the group consisting of $PF_6^-$, $AsF_6^-$, $SbF_6^-$, $AlCl_4^-$, $HSO_4^-$, $ClO_4^-$, $CH_3SO_3^-$, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, said halide ion and said carboxylic acid ion having a total of 1 to 3 carbons.

13. The method of dissolving nucleic acids of claim 11 or 12, wherein said anion is selected from the group consisting of said halide ion and said carboxylic acid ion having a total of 1 to 3 carbons.

14. The method of dissolving nucleic acids of claim 11 or 12, wherein the ionic liquid is a neutralized ionic liquid.

## (IX) EVIDENCE APPENDIX

None presented.

## (X) **RELATED PROCEEDINGS APPENDIX**

No related proceedings.